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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,785	04/06/2001	Patrick Florent	B45096C1	7816

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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	4

DATE MAILED: 05/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,785	FLORENT ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09284887* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1 and 3-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1, the applicant has used multiple possible ranges f concentrations for each of the vaccine constituents. The other claims are indefinite as depending from claim 1. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites, for example, the broad recitation the diphtheria (D) concentration does not exceed 5 Lf. However, the claim also recites that the diphtheria concentration is "preferably I-4 Lf, more preferably about 2 Lf," all of which are

narrower statements of the range limitation. The same recitation format is also given for tetanus (T), and the Pertussis antigens- pertussis toxoid (PT), filamentous hemagglutinin (FHA), and pertactin (69K). As one who was reading the claim would not know which range of concentrations the claim required for any of the constituents, the claim is indefinite.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feery et al, Med. J. Aust. 1:128-30 (Feery) in view of Edwards et al, Ped. Vol. 96 supp., pp. 548-57 (1995). For the purposes of this rejection, claim 1 is being read as encompassing the broadest concentration ranges of vaccine compositions. Thus, claim 1 describes a .5 ml dose of a DTP comprising antigens as described as follows: D does not exceed 5Lf, T does not exceed 10 Lf, PT does not exceed 10 μg, FHA does not exceed 10 μg, and 69K does not exceed 4μg.

Feery teaches a Diphtheria Tetanus vaccine that comprises 5 Lf of tetanus toxin and 2 Lf of diphtheria toxin when measured for a .5 ml dose. P. 129, col. 1. The reference is describing a study done to determine if reduced diphtheria toxin dosages may be used in diphtheria toxin containing vaccines. P. 128, col. 2. Thus, the study teaches that any vaccine that is targeting diphtheria, either alone or with other antigens, may use the tetanus and diphtheria dosages described therein. However, Feery does not teach a DTP vaccine.

Edwards teaches DTP vaccines wherein diphtheria is generally at concentration greater than ten, and shows that most vaccines comprising tetanus and diphtheria contain diphtheria at a higher dosage than it does tetanus. See, Table 1, p. 549. In Table 1, Edwards also describes a DTP vaccine from Biocine known as BSc-3P (Biocine). Biocine contains all of the antigens required by claim 1. Although Edward discloses PT, FHA, and 69K (PRN in Table 1), in concentrations within the ranges required by clam 1, the disclosed concentrations of diphtheria and tetanus are too high. Id.

One of ordinary skill in the art would have known- given the disclosure by Feery, to combine Feery's low TD dosages with other vaccines. Thus, one of ordinary skill in the art would have been lead to use Feery's dosages in any on the DTP vaccines then known to work, including Biocine. Combining the low dosages of diphtheria and tetanus of Feery with Biocine's dosages of PT, FHA, and 69K, one gets a vaccine fulfilling the requirements of claim 1. The motivation to do so would be to reduce the likelihood of Arthus-type reactions discussed in Feery (caused by diphtheria toxoid at higher dosages). Feery, p. 128, col. 2. As both the lower dosages of diphtheria and tetanus were known to work due to Feery, and the pertussis vaccine contained in Biocine were known to work, one of ordinary skill in the art would have had a reasonable expectation that the new DTP vaccine would work.

The method of clam 9 would be obvious to one of ordinary skill in the art once the vaccine of claim 1 was derived.

5. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Feery in view of Edwards. Claim 2 describes a multivalent vaccine comprising the following constituents at the stated concentrations in a .5 ml dosage: PT- 8μg, FHA – 8μg, 69K- 2.5μg, D- 2Lf, and T- 5Lf.

Feery teaches a DT vaccine that may be used with other vaccines wherein the concentration of tetanus is 5Lf and the concentration of diphtheria is 2Lf. As stated above, the reference also teaches that this vaccine may be used in combination with other vaccine compositions. It does not teach specific concentration of other antigens.

Edwards describes several DTP vaccines known in the art, including the concentrations of various pertussis antigens used in DTP vaccines. The reference shows vaccines wherein the concentrations of PT range from 3.5 to 50 μg, including several vaccines of 5 or 10 μg; those of FHA range from 2.5 to 35 μg, including vaccines with 5 and 10 μg; and those of 69K range from 2 to 8μg, including a vaccine with concentration of 2.5 μg. p. 549, Table 1. Included in the list are vaccines wherein the concentration of 69K is between than 2 and 3μg, and the concentrations of both PT and FHA are both between 5 and 10μg. Thus, it would have been obvious to one of ordinary skill in the art to make a pertussis vaccine with the concentrations as described in claim 2, since the concentrations described by the claim fall with the ranges prescribed by the prior art. Because the concentrations are similar to those in the prior art, one of ordinary skill in the art would have had a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to combine the pertussis vaccine of the claimed concentrations with the Feery diphtheria and tetanus vaccine for the reasons stated in the rejection of ¶4 above.

6. Claims 1, 3-8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feery, and Edwards, and further in view of Petre et al, PCT/EP93/01276 (Petre) and Eckhardt et al. U.S. Patent Number 5,895,655 (the '655 patent). These claims describe a DTP vaccine (and a method of using it) that may be combined with one or more other antigens, such as Hepatitis B (HB), especially the S-antigen of Hepatitis B surface antigen (HBsAg). The vaccine may also contain Haemophilius influenza (Hib), polio, or Hepatitis A(HA). the claims further recite that the combined vaccine be made with an adjuvant of either aluminum hydroxide or aluminum phosphate.

As described above, Feery and Edwards teach a DTP vaccine as per claim 1. In Feery, the vaccine included an adjuvant of aluminum phosphate. P. 129, col. 2. In Edwards, the multiple vaccines used a variety of adjuvants, including aluminum phosphate and aluminum hydroxide. P. 550. However, the two references do not specifically teach the use of additional antigens. (As mentioned above, Feery does teach that the vaccine disclosed therein may be used with other antigens.)

Petre teaches a Hepatitis B (HB) vaccine that may be combined with one or more other antigens, such as HA, diphtheria, tetanus, acellular pertussis, Hib, and polio. P. 1, lines 19-24. Petre uses a vaccine comprising HB surface antigen as an example. P. 1, lines 8-12. The reference further teaches that commonly used vaccine adjuvants include both aluminum hydroxide and aluminum phosphate. P.1, lines 25-38. Thus, Petre teaches all the elements of the dependant claims 3-9, except for the DTP vaccine of claim 1.

The '655 patent teaches the creation of a multivalent vaccine comprising a pertussis vaccine in combination with antigens against other infections. Col. 3, lines 58-67. The patent

teaches that one of ordinary skill in the art would be motivated to combine vaccines in order to reduce the number of dosage administrations needed to provide protection against the various infections. Id.

Given the Feery, Edwards combination, and the disclosures of Petre and the '655 patent, it would have been obvious to one of ordinary skill in the art to combine the references to create a multivalent vaccine comprising DTP, HBsAg, and one or more of Hib, polio, or HA. Because Feery teaches that its vaccine may be combined with others (see above), and because Petre also teaches that HBsAg may be combined with other vaccines, one of ordinary skill in the art would have had no reason to believe that any of the vaccines would be less effective due to the combinations.

Conclusion

7. The examiner notes that a PTO-1449 and two PTO form 892s from a parent application have been filed, and the references duly examined by the examiner. However, unless a PTO-1449 for the present applicant is filed, the references in those filings will not be made of record in the present case.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
May 10, 2002

JAMES HOUSEL 5/20/02
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